(FILE 'HOME' ENTERED AT 17:33:04 ON 21 DEC 1999)

FILE 'EMBASE, MEDLINE, BIOSIS, CAPLUS, CANCERLIT, SCISEARCH, TOXLINE, APIPAT, CROPU, DGENE, DPCI, EUROPATFULL, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE, PATOSEP, PATOSWO, PIRA, RAPRA, TULSA, TULSA2, USPATFULL' ENTERED AT 17:34:12 ON 21 DEC 1999

L1 227915 S (CCA OR CELL CYCLE ARREST OR APOPTOSIS OR APOPTOTIC)
L2 25338 S (DIMER OR CONJUGATE OR CROSSLINK##) (10A) (AB OR ANTIBODY OR
L3 36 S L1 (30A) L2
L4 21 DUP REM L3 (15 DUPLICATES REMOVED)

=> s l4 and (cd19 or cd19 or b4 or her2)

12 FILES SEARCHED...

L5 ANSWER 1 OF 2 USPATFULL
AN 1999:67016 USPATFULL
TI EGF-genistein conjugates for the treatment of cancer
IN Uckun, Fatih M., White Bear Lake, MN, United States
PA Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation)
PI US 5911995 19990615
AI US 1996-602186 19960216 (8)
RLI Continuation-in-part of Ser. No. US 1994-293731, filed on 19 Aug 1994, now patented, Pat. No. US 5587459
DT Utility
LN.CNT 1209
INCL INCLM: 424/195.110
INCLS: 424/185.100; 424/192.100; 424/193.100; 530/391.700; 514/002.000; 514/004.000
NCL NCLM: 424/195.110
NCLS: 424/185.100; 424/192.100; 424/193.100; 514/002.000; 514/004.000; 530/391.700
IC [6]
ICM: A61K039-385
ICS: A61K039-00; C07K016-00; A01N061-00
EXF 530/391.1; 530/391.7; 530/391.9; 530/388.75; 530/325; 530/345; 424/181.1; 424/195.11; 424/185.1; 424/192.1; 424/193.1; 514/4; 514/12; 514/2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 2

L5 ANSWER 2 OF 2 USPATFULL
AN 97:104105 USPATFULL
TI Epitope-specific monoclonal antibodies and immunotoxins and uses thereof
IN Uhr, Jonathan W., Dallas, TX, United States
Vitetta, Ellen S., Dallas, TX, United States
Scheuermann, Richard H., Carrollton, TX, United States
PA Board of Regents, The University of Texas, Austin, TX, United States (U.S. corporation)
PI US 5686072 19971111
AI US 1994-202042 19940222 (8)
RLI Continuation-in-part of Ser. No. US 1992-899781, filed on 17 Jun 1992, now abandoned
DT Utility
LN.CNT 2395
INCL INCLM: 424/183.100
INCLS: 530/391.700; 530/388.730; 435/007.240
NCL NCLM: 424/183.100
NCLS: 435/007.240; 530/388.730; 530/391.700
IC [6]
ICM: A61K039-395
EXF 424/183.1; 530/391.7; 530/388.73; 435/7.24

L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 1999 ACS
AN 1999:487328 CAPLUS
DN 131:115312
TI Antibodies to death receptor 4 (DR4) and uses thereof
IN Chuntharapai, Anan; Kim, Kyung Jin
PA Genentech, Inc., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9937684	A1	19990729	WO 1999-US1437	19990125
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9923382	A1	19990809	AU 1999-23382	19990125

PRAI US 1998-PV72481 19980126
US 1998-72481 19980126
WO 1999-US1437 19990125

AB Death Receptor 4 (DR4) antibodies are provided. DR4 antibodies are capable of modulating biol. activities assocd. with Apo-2 ligand, in particular, apoptosis, and thus are useful in the treatment of various diseases and pathol. conditions including cancer. The DR4 antibodies may be included in pharmaceutical compns., articles of manuf., or kits. Methods of treatment and diagnosis using the DR4 antibodies are also provided.

IT Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DR4 **antibody dimer**; antibodies to death receptor 4 for modulating Apo-2 ligand-assocd. **apoptosis** and for treatment and diagnosis of diseases including cancer)

L4 ANSWER 2 OF 21 USPATFULL
AN 1999:132512 USPATFULL
TI Method of detecting apoptosis using an anti-human GP46 monoclonal anti-body
IN Desjardins, Louise, 1139 St. Jovite Ridge, Gloucester, Ontario, Canada K1C 1Y6
PI US 5972622 19991026
AI US 1997-796841 19970206 (8)
PRAI US 1996-11324 19960208 (60)
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Bansal, Geetha P.
LREP Sterne, Kessler, Goldstein & Fox P.L.L.C.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1,8
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1275
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to antibodies or fragments thereof that can be used as indicators of apoptosis. More specifically this invention relates to antibodies and fragments thereof that selectively bind GP46, a protein whose levels increase significantly upon induction of apoptosis. This invention also relates to the hybridomas that produce anti-GP46 monoclonal antibodies. This invention also discloses a method of detecting cell death by apoptosis in vitro or in vivo by detecting and quantifying GP46 present in biological samples, comprising contacting the sample with the antibodies or fragments to form GP46 immunocomplexes, which may then be detected by the use of known methods.

This detection method is useful for research into apoptosis and research relating to diseases in which apoptosis is involved. This method could also be used to diagnose the extent of damage caused by a particular disease or to evaluate the efficacy of drug treatments. The present invention also relates to a method of using the anti-GP46 antibodies or fragments in nuclear medical imaging. The present invention further relates to therapeutic uses of the anti-GP46 antibodies or fragments. The antibodies or fragments can also be incorporated into kits for the detection of apoptosis.

SUMM The present invention also relates to a method for the detection of sites of **apoptosis** in a patient, which comprises preparing a medically-useful **antibody conjugate** comprising an anti-GP46 **antibody** or fragment thereof and a medically-useful label; administering a safe and effective amount of the medically-useful antibody conjugate to the. . .

DETD In this method, the **antibody**- or fragment-therapeutic agent **conjugate** can be delivered to the site of **apoptosis** thereby directly exposing the **apoptotic** cells to the therapeutic agent.

L4 ANSWER 3 OF 21 USPATFULL
AN 1999:121553 USPATFULL
TI Antibodies to protein, FAF1
IN Chu, Keting, Burlingame, CA, United States
Williams, Lewis T., Tiburon, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5962652 19991005
AI US 1997-993210 19971218 (8)
RLI Division of Ser. No. US 1995-477476, filed on 7 Jun 1995, now patented, Pat. No. US 5750653
DT Utility
EXNAM Primary Examiner: Mertz, Prema
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 1909
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention identifies a novel, Fas-associated factor 1 termed FAF1 which potentiates Fas-induced cell killing. The invention provides FAF1 nucleic acid and polypeptide compositions as well as methods of using these compositions in the therapeutic treatment of diseases resulting from dysregulation in apoptosis. Also provided are cells carrying and expressing the nucleic acid compositions and methods of using these cells to screen for agonists and antagonists of Fas-mediated apoptosis. Methods of isolating FAF1-interacting proteins are disclosed.

Also provided are antibodies that bind FAF1, a hybridoma and a kit comprising the antibodies.

DETD . . . presence of the test molecule will be tested for eg. for

disruption of Fas-FAF1 interaction or for any effect on **apoptosis** with or without stimulation of Fas. In one embodiment, the cells are **crosslinked** with anti-CD4 **antibody** (e.g., L3T4) and then assayed for any effects on FAF1 activity essentially as described in the Experimental Examples under the. . .

DETD . . . wild type (CD4/fas) or mutant (CD4/fas786A) chimeric molecules were chosen for analysis (FIGS. 1A-1D). L cells expressing CD4/fas (CD4/fas-16 underwent **apoptotic** cell death when **crosslinked** by **monoclonal antibody** against CD4 (L3T4, Caltag)) in the presence of actinomycin D (Itoh et al., DNA Cloning, a Practical Approach, IRL Press,. . .

L4 ANSWER 4 OF 21 USPATFULL
AN 1999:92519 USPATFULL
TI Monoclonal antibody that detects apoptotic antigen
IN Schlossman, Stuart Franklin, Newton Centre, MA, United States
Zhang, Chonghui, Brookline, MA, United States
PA Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
PI US 5935801 19990810
AI US 1996-623876 19960329 (8)
DT Utility
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Nolan, Patrick J.
LREP Alter, Mitchell E.
CLMN Number of Claims: 8
ECL Exemplary Claim: 6
DRWN 18 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 888
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A monoclonal antibody which specifically binds to an antigen on the membrane of mitochondria in apoptotic cells. The antigen is a 38 kD protein that is detectable in cells undergoing apoptosis and undetectable in normal cells. This selectivity of the monoclonal antibody provides a method of distinguishing between normal and apoptotic cells in a sample of human hemopoietic cell populations. A method for detecting and measuring cells undergoing apoptosis is also provided.
DRWD . . . the ELISA test of cell lysates prepared from normal or apoptotic Jurkat cells. Cell lysates were prepared from normal or **apoptotic** Jurkat cells induced by .gamma.-irradiation or Ara-C treatment, and precoated onto ELISA plates. The plates were incubated with anti-7A6 or an isotype-matched control **antibody**, followed by goat anti-mouse IgG-peroxidase **conjugate**. The enzymatic reaction was developed by orthophenylenediamine substrate and read at 492 nM using an ELISA reader.

L4 ANSWER 5 OF 21 USPATFULL
AN 1999:67016 USPATFULL
TI EGF-genistein conjugates for the treatment of cancer
IN Uckun, Fatih M., White Bear Lake, MN, United States
PA Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation)
PI US 5911995 19990615
AI US 1996-602186 19960216 (8)
RLI Continuation-in-part of Ser. No. US 1994-293731, filed on 19 Aug 1994, now patented, Pat. No. US 5587459
DT Utility
EXNAM Primary Examiner: Huff, Sheela; Assistant Examiner: Eyler, Yvonne
LREP Merchant, Gould, Smith, Edell, Welter & Schmidt, P.A.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1209

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A conjugate formed of epidermal growth factor covalently linked to a tyrosine kinase inhibitor, such as genistein, and a method for killing cancer cells, in vivo and in vitro, by administering a cytotoxic dose of an epidermal growth factor tyrosine kinase inhibitor conjugate.
DETD . . . antibody as a carrier molecule. As described in co-pending U.S. patent application Ser. No. 08/293,731, applicant has shown that genistein **conjugate** of B43 (anti-CD19) **monoclonal antibody** triggers **apoptotic** cell death in childhood leukemia cells.

L4 ANSWER 6 OF 21 EUROPATFULL COPYRIGHT 1999 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

AN 884385 EUROPATFULL ED 19990103 EW 199851 FS OS
TIEN Intracellular modulators of apoptopic cell death pathways.
TIDE Intrazellulaere Modulatoren fuer apoptopischen Zelltotwegen.
TIFR Modulateurs intracellulaires des voies de mort cellulaire apoptopique.
IN Riccardo Carlo, Via del Favarone,37, 06100 Perugia, IT
PA APPLIED RESEARCH SYSTEMS ARS HOLDING N.V., 14 John B. Gorsiraweg, Curacao, AN
PAN 1180075
AG Pieraccioli, Daniele, Istituto Farmacologico Serono SpA Via Casilina, 125, 00176 Roma, IT
AGN 80461
OS ESP1998088 EP 0884385 A1 981216
SO Wila-EPZ-1998-H51-T1a
DT Patent
LA Anmeldung in Englisch; Veroeffentlichung in Englisch
DS R IT
PIT EPA1 EUROPAEISCHE PATENTANMELDUNG
PI EP 884385 A1 19981216
OD 19981216
AI EP 1997-107033 19970428
ABEN A DNA sequence encoding a glucocorticoid-induced leucine-zipper family related protein (GILR), isoforms, fragments or analogs thereof said GILR, isoforms, fragments or analogs thereof capable of inhibiting apoptosis and stimulating lymphocyte activity, GILR proteins, isoforms, analogs, fragments and derivatives thereof encoded by the aforesaid DNA sequence, their preparation and uses.

DETDEN. . . same transfected clones are protected only to a significantly lesser extent against the programmed cell death induced with other typical **apoptotic** agents such as DEX, UV irradiation, serum starvation or triggering of Fas by **crosslinked** anti-Fas **mAb**.
It . . . the same clones (results with GILR/1,5,7 and pcDNA3/4,7,8 are shown in Fig. 7) indicate that GILR overexpression does not counteract **apoptosis** induced by DEX, various doses of UV irradiation, starvation or triggering by **crosslinked** anti-Fas **mAb**.
It . . . al, 1995; Dhein et al., 1995; Ju et al., 1995). In particular, the present inventors have previously shown that anti-CD3-induced **apoptosis** in 3DO cells is blocked by soluble anti-Fas **mAb** while **crosslinked** anti-Fas **mAb** directly induces cell death (Ayroldi et al, 1997). Experiments were performed to test whether blocking of Fas (using soluble, non-**crosslinked** anti-Fas **mAb**, 1.mu.g/ml) could inhibit the anti-CD3-induced **apoptosis** in this experimental system where clones of 3DO were tested. Results indicate that blocking of Fas significantly inhibits CD3-induced cell. . .

L4 ANSWER 7 OF 21 USPATFULL

AN 1998:150653 USPATFULL
TI Inhibition of APC-mediated apoptosis of activated T lymphocytes
IN Schlossman, Stuart F., Newton, MA, United States
Wu, Mei X., Cambridge, MA, United States
PA Dana-Farber Cancer Institute, Inc., Boston, MA, United States (U.S. corporation)
PI US 5843635 19981201
AI US 1995-395149 19950227 (8)
DT Utility
EXNAM Primary Examiner: Achutamurthy, Ponnathapura; Assistant Examiner: Park, Hankyel T.
LREP Weingarten, Schurgin, Gagnebin & Hayes LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 818
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for interfering with antigen presenting cell-mediated priming of resting peripheral blood T lymphocytes to undergo activation induced cell death ("apoptosis") by inhibiting an interaction between a membrane associated molecule ("an APC apoptotic ligand") present on stimulated antigen presenting cells ("APC") and a counter-receptor that is present on T lymphocytes are disclosed. The antigen presenting cells are preferably from the monocyte/macrophage cell line or are dendritic cells. Also disclosed are methods of screening for inhibitors of APC-mediated priming of T lymphocytes to undergo apoptosis and methods and agents for detecting, identifying and characterizing an APC apoptotic ligand. Inhibitors identified by the screening method of the invention are used to reduce the T lymphocyte depletion associated with HIV infection and thereby mitigate the severe immunodeficiency associated with AIDS by interfering with the association between HIV-infected antigen presenting cells, especially monocytes and macrophages, and T cells.
DETD . . . to T cells can be found (Embretson et al., Nature 362:359-362 1993). These T cells would be particularly susceptible to **apoptosis** upon further stimulation as might occur following antigen recognition, superantigen binding, CD4 molecule crosslinking by membrane associated gp160 on the infected macrophages, and/or CD4 **crosslinked** by gp120 in the presence of anti-gp120 **Ab**. Such a process could result in the continuous and slow depletion of CD4.sup.+ cells and even of those activated CD8.sup.+. . .

L4 ANSWER 8 OF 21 USPATFULL
AN 1998:134631 USPATFULL
TI Fas antagonists and uses thereof
IN Lynch, David H., Bainbridge Island, WA, United States
Alderson, Mark R., Bainbridge Island, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI US 5830469 19981103
AI US 1995-429499 19950426 (8)
RLI Continuation-in-part of Ser. No. US 1994-322805, filed on 13 Oct 1994, now patented, Pat. No. US 5620889 which is a continuation-in-part of Ser. No. US 1993-159003, filed on 29 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-136817, filed on 14 Oct 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Loring, Susan A.
LREP Anderson, Kathryn A.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1997
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a panel of monoclonal antibodies and

binding proteins which specifically bind to human Fas antigen. Some of the antibodies and binding proteins are capable of stimulating T cell proliferation, inhibiting binding of anti-Fas CH-11 monoclonal antibody to cells expressing Fas antigen, blocking anti-Fas CH-11 monoclonal antibody-mediated lysis of cells, and blocking Fas ligand-mediated lysis of cells. The invention also provides for therapeutic compositions comprising the monoclonal antibodies.

DETD . . . an overnight .sup.51 Cr-release assay was used to measure cell lysis induced by huFas monoclonal antibodies. The ability to induce **apoptosis** in Fas bearing target cells was determined for the IgG1 isotype Fas **monoclonal** antibodies when the antibodies were added in solution and when **crosslinked**, i.e., bound to the plastic of tissue culture plates. The data collected are summarized in Table 1. Some of the. . .

L4 ANSWER 9 OF 21 USPATFULL
AN 1998:51729 USPATFULL
TI Protein, FAF1, which potentiates Fas-mediated apoptosis and uses thereof
IN Chu, Keting, Burlingame, CA, United States
Williams, Lewis T., Tiburon, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5750653 19980512
AI US 1995-477476 19950607 (8)
DT Utility
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Basham, Daryl A.
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 33 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 1869
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention identifies a novel, Fas-associated factor 1 termed FAF1 which potentiates Fas-induced cell killing. The invention provides FAF1 nucleic acid and polypeptide compositions as well as methods of using these compositions in the therapeutic treatment of diseases resulting from dysregulation in apoptosis. Also provided are cells carrying and expressing the nucleic acid compositions and methods of using these cells to screen for agonists and antagonists of Fas-mediated apoptosis. Methods of isolating FAF1-interacting proteins are disclosed.

DETD . . . presence of the test Molecule will be tested for e.g. for disruption of Fas-FAF1 interaction or for any effect on **apoptosis** with or without stimulation of Fas. In one embodiment, the cells are **crosslinked** with anti-CD4 **antibody** (e.g., L3T4) and then assayed for any effects on FAF1 activity essentially as described in the Experimental Examples under the. . .

DETD . . . wild type (CD4/fas) or mutant (CD4/fas786A) chimeric molecules were chosen for analysis (FIG. 1A). L cells expressing CD4/fas (CD4/fas-16 underwent **apoptotic** cell death when **crosslinked** by **monoclonal antibody** against CD4 (L3T4, Caltag)) in the presence of actinomycin D (Itoh et al., DNA Cloning, a Practical Approach, IRL Press,. . .

L4 ANSWER 10 OF 21 MEDLINE DUPLICATE 1
AN 1998421154 MEDLINE
DN 98421154
TI Essential requirement for caspase-8/FLICE in the initiation of the Fas-induced apoptotic cascade.
AU Juo P; Kuo C J; Yuan J; Blenis J
CS Department of Cell Biology, Harvard Medical School, Boston, Massachusetts

02115, USA.
SO CURRENT BIOLOGY, (1998 Sep 10) 8 (18) 1001-8.
Journal code: B44. ISSN: 0960-9822.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
EW 19990204
AB BACKGROUND: Fas (APO-1/CD95) is a member of the tumor necrosis factor receptor (TNF-R) family and induces **apoptosis** when **crosslinked** with either Fas ligand or agonistic **antibody** (Fas **antibody**). The Fas-Fas ligand system has an important role in the immune system where it is involved in the downregulation of immune responses and the deletion of peripheral autoreactive T lymphocytes. The intracellular domain of Fas interacts with several proteins including FADD (MORT-1), DAXX, RIP, FAF-1, FAP-1 and Sentrin. The adaptor protein FADD can, in turn, interact with the cysteine protease caspase-8 (FLICE/MACH/Mch5). RESULTS: In a genetic screen for essential components of the Fas-mediated apoptotic cascade, we isolated a Jurkat T lymphocyte cell line deficient in caspase-8 that was completely resistant to Fas-induced apoptosis. Complementation of this cell line with wild-type caspase-8 restored Fas-mediated apoptosis. Fas activation of multiple caspases and of the stress kinase p38 and c-Jun NH2-terminal kinase (JNK) was completely blocked in the caspase-8-deficient cell line. Furthermore, the cell line was severely deficient in cell death induced by TNF-alpha and was partially deficient in cell death induced by ultraviolet irradiation, adriamycin and etoposide. CONCLUSIONS: This study provides the first genetic evidence that caspase-8 occupies an essential and apical position in the Fas signaling pathway and suggests that caspase-8 may participate broadly in multiple apoptotic pathways.
AB BACKGROUND: Fas (APO-1/CD95) is a member of the tumor necrosis factor receptor (TNF-R) family and induces **apoptosis** when **crosslinked** with either Fas ligand or agonistic **antibody** (Fas **antibody**). The Fas-Fas ligand system has an important role in the immune system where it is involved in the downregulation of. . .

L4 ANSWER 11 OF 21 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 2
AN 1998261470 EMBASE
TI Fas/Fas ligand and hematopoietic progenitor cells.
AU Niho Y.; Asano Y.
CS Dr. Y. Niho, First Department Internal Medicine, Faculty of Medicine, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-82, Japan
SO Current Opinion in Hematology, (1998) 5/3 (163-165).
Refs: 23
ISSN: 1065-6251 CODEN: COHEF4
CY United States
DT Journal; (Short Survey)
FS 025 Hematology
029 Clinical Biochemistry
LA English
SL English
AB Fas antigen is a receptor that **crosslinks** with a ligand or **antibody** initiating a signal transduction cascade that leads to **apoptosis**. During normal hematopoiesis, Fas antigen is not expressed on CD34+ cells, including premature hematopoietic progenitor cells. Functional Fas antigen expression is induced by several hematopoietic regulators. These changes may appear not only in the process of differentiation of hematopoietic progenitor cells, but also as a negative feedback mechanism that controls chaotic proliferation of these cells. These findings suggest that the Fas/Fas ligand system is closely related to the maintenance of homeostasis during the process of normal hematopoiesis. Furthermore, increased Fas antigen expression is observed

on CD34+ cells fro[redacted]atients with aplastic anemia, s[redacted]gesting that it might cause bone marrow suppression. The use of Fas-[redacted]diated apoptosis of malignant cells as a tool for eliminating hematologic malignancies is promising. Increased Fas ligand expression is observed on natural killer lymphoma cells and may be associated with the pathogenesis of failure of several organs. The Fas/Fas ligand system plays an important role in the physiologic and pathologic processes of hematopoiesis. The development of treatments using this system are forthcoming.

AB Fas antigen is a receptor that **crosslinks** with a ligand or **antibody** initiating a signal transduction cascade that leads to **apoptosis**. During normal hematopoiesis, Fas antigen is not expressed on CD34+ cells, including premature hematopoietic progenitor cells. Functional Fas antigen expression. . .

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 1999 ACS
AN 1997:809900 CAPLUS
DN 128:75636
TI Preparation of branched galactosamine-biotin conjugates as cluster clearing agents
IN Theodore, Louis J.; Axworthy, Donald B.
PA Neorx Corporation, USA
SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746098	A1	19971211	WO 1997-US9394	19970606
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2257363	AA	19971211	CA 1997-2257363	19970606
	EP 914042	A1	19990512	EP 1997-928760	19970606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1996-659761		19960606		
	WO 1997-US9394		19970606		

OS MARPAT 128:75636

AB Cluster clearing agents (CCAs), agents that impact the elimination and biodistribution of constructs in a manner resulting in increased elimination via a hepatic route, and the use thereof are discussed. CCAs are composed of a hepatic clearance directing moiety which directs the biodistribution of a CCA-contg. construct to hepatic clearance; and a binding moiety which mediates binding of the CCA to a compd. for which rapid hepatic clearance is desired. Branched galactosamine-biotin conjugates, e.g. I, were prepd. by std. chem. coupling procedures. The prepd. branched galactosamine-biotin conjugate CCAs were evaluated by treating tumor-bearing mice initially with a NR-LU-10 **monoclonal antibody**-streptavidin **conjugate**, followed by the **CCA** after 24 h, and finally administration of an 111In-DOTA-biotin conjugate after 2, 4, 8, or 24 h. Blood levels of the 111In-DOTA-biotin decreased as the 2nd time interval above increased, apparently correlating with a decrease in circulating NR-LU-10-streptavidin levels. The lack of CCA tumor comprise, even at 24 h, was encouraging, and the enhanced blood clearance of the conjugate over this extended time allowed the achievement of markedly improved tumor/blood ratios. Thus, the prepd. CCAs offer a variety of novel dosing applications which can be exploited to improve blood (and presumably, whole body) clearance of 111In-DOTA-biotin without sacrificing tumor uptake.

AB . . . std. chem. coupling procedures. The prepd. branched galactosamine-biotin conjugate CCAs were evaluated by treating tumor-bearing mice initially with a NR-LU-10 **monoclonal antibody**-streptavidin **conjugate**, followed by the

CCA after 24 h, an[redacted]inally administration of an 11[redacted]-DOTA-biotin conjugate after 2, [redacted], 8, or 24 h. Blood levels of.[redacted] .

L4 ANSWER 13 OF 21 USPATFULL
AN 97:104105 USPATFULL
TI Epitope-specific monoclonal antibodies and immunotoxins and uses thereof
IN Uhr, Jonathan W., Dallas, TX, United States
Vitetta, Ellen S., Dallas, TX, United States
Scheuermann, Richard H., Carrollton, TX, United States
PA Board of Regents, The University of Texas, Austin, TX, United States (U.S. corporation)
PI US 5686072 19971111
AI US 1994-202042 19940222 (8)
RLI Continuation-in-part of Ser. No. US 1992-899781, filed on 17 Jun 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Scheiner, Toni R.
LREP Arnold White & Durkee
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 2395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The anti-tumor activity of a mixture of anti-CD22 and anti-CD19 immunotoxins is shown to be significantly enhanced in SCID/Daudi mice with disseminated human Daudi lymphoma. Unexpectedly identical enhancement was observed employing a combination of the anti-CD22 immunotoxin with unconjugated anti-CD19 antibodies. Thus combinations of an anti-CD22 immunotoxin and an anti-CD19 immunotoxin or antibody act synergistically and provide advantageous compositions and methods for immunotherapeutic treatment of various diseases including cancer and autoimmune disorders. Also disclosed is data indicating that certain anti-CD19 antibodies alone inhibit proliferation of CD19-positive cells by inducing cell cycle arrest.
SUMM . . . CD19.sup.+ B cell, comprising: contacting CD19.sup.+ B cells with an anti-CD19 antibody that binds to the epitope recognized by the **antibody** HD37, or a fragment or **conjugate** thereof, in an amount effective to inhibit the proliferation in said CD19.sup.+ B cells. Alternatively the effect of the anti-CD19 on the B cell may be induction of **cell cycle arrest**. In a more preferred embodiment the anti-CD19 **antibody** comprises the anti-CD19 **antibody** HD37, or a fragment or **conjugate** thereof. Also in a preferred embodiment the anti-CD19 **antibody** comprises the anti-CD19 antibody BU12, or a fragment or **conjugate** thereof. In an alternative embodiment the anti-CD19 antibody comprises the anti-CD19 antibody 4G7, or a fragment or conjugate thereof. In. . .

L4 ANSWER 14 OF 21 USPATFULL
AN 97:31611 USPATFULL
TI Human anti-Fas IgG1 monoclonal antibodies
IN Lynch, David H., Bainbridge Island, WA, United States
Alderson, Mark R., Bainbridge Island, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI US 5620889 19970415
AI US 1994-322805 19941013 (8)
RLI Continuation-in-part of Ser. No. US 1993-159003, filed on 29 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-136817, filed on 14 Oct 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Loring, Susan A.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 10 Drawing Page(s)

LN.CNT 1698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a panel of monoclonal antibodies and binding proteins which specifically bind to human Fas antigen. Some of the antibodies and binding proteins are capable of stimulating T cell proliferation, inhibiting binding of anti-Fas CH-11 monoclonal antibody to cells expressing Fas antigen, blocking anti-Fas CH-11 monoclonal antibody-mediated lysis of cells, and blocking Fas ligand-mediated lysis of cells. The invention also provides for therapeutic compositions comprising the monoclonal antibodies.
DETD . . . an overnight .sup.51 Cr-release assay was used to measure cell lysis induced by huFas monoclonal antibodies. The ability to induce **apoptosis** in Fas bearing target cells was determined for the IgG1 isotype Fas **monoclonal** antibodies when the antibodies were added in solution and when **crosslinked**, i.e., bound to the plastic of tissue culture plates. The data collected are summarized in Table 1. Some of the. . .

L4 ANSWER 15 OF 21 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 3
AN 1996:525072 BIOSIS
DN PREV199699247428
TI Enhancement of CD3-mediated thymocyte apoptosis by the cross-linkage of heat-stable antigen.
AU Hitsumoto, Y. (1); Song, D.-S.; Okada, M.; Hamada, F.; Saheki, S.; Takeuchi, N.
CS (1) Dep. Clinical Lab. Med., Ehime Univ. Sch. Med., Shigenobu, Onsen-gun, Ehime 791-02 Japan
SO Immunology, (1996) Vol. 89, No. 2, pp. 200-204.
ISSN: 0019-2805.
DT Article
LA English
AB Heat-stable antigen (HSA) is a murine differentiating antigen that is expressed on both CD4-CD8- double-negative and CD4+CD8+ double-positive thymocytes but not CD4+ or CD8+ single-positive thymocytes. Effects of anti-HSA monoclonal antibody, R13, on thymocyte apoptosis induced by various stimulations were investigated by a single-cell suspension culture system. Immobilized R13 enhanced the CD3-mediated DNA fragmentation and killing of thymocytes but not the dexamethasone-induced or phorbol myristate acetate-induced killing of thymocytes. Immobilized R13 by itself could not induce thymocyte **apoptosis**. Soluble R13 enhanced CD3-mediated **apoptosis** when HSA and T-cell receptor (TCR)/CD3 were co-**crosslinked** by a cross-reactive secondary **antibody**. Even without the cross-reactive secondary antibody, soluble R13 enhanced CD3-mediated **apoptosis**, although a greater than 100-fold increase in the amount of R13 was needed to give a similar enhancement compared with immobilized R13. Neither R13 by itself nor R13 plus secondary antibody induced cytosolic calcium influx, whereas R13 enhanced CD3-mediated cytosolic calcium increase. These results suggest a functional role of HSA in promoting the activation-induced apoptosis of thymocytes and the involvement of HSA in negative selection.
AB. . . thymocytes but not the dexamethasone-induced or phorbol myristate acetate-induced killing of thymocytes. Immobilized R13 by itself could not induce thymocyte **apoptosis**. Soluble R13 enhanced CD3-mediated **apoptosis** when HSA and T-cell receptor (TCR)/CD3 were co-**crosslinked** by a cross-reactive secondary **antibody**. Even without the cross-reactive secondary antibody, soluble R13 enhanced CD3-mediated **apoptosis**, although a greater than 100-fold increase in the amount of R13 was needed to give a similar enhancement compared with. . .

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 1999 ACS
AN 1996:54871 CAPLUS

DN 124:114962
TI Antibody-targeted superantigen therapy induces tumor-infiltrating lymphocytes, excessive cytokine production, and apoptosis in human colon carcinoma
AU Litton, Mark J.; Dohlsten, Mikael; Lando, Peter A.; Kalland, Terje; Ohlsson, Lennart; Andersson, Jan; Andersson, Ulf
CS Dep. Immunology, Univ. Stockholm, Stockholm, Swed.
SO Eur. J. Immunol. (1996), 26(1), 1-9
CODEN: EJIMAF; ISSN: 0014-2980
DT Journal
LA English
AB Bacterial superantigens are the most potent known activators of human T lymphocytes. To engineer superantigens for immunotherapy of human colon carcinoma, the superantigen, staphylococcal enterotoxin A (SEA) was genetically fused to the Fab region of the colon carcinoma-reactive monoclonal antibody C242. In the present study the effector mechanisms involved in the anti-tumor response to C242 Fab-SEA were characterized. Immunohistochem. and computer-aided image anal. were used in studies of cryopreserved tumor tissue to evaluate the phenotype of infiltrating cells and their cytokine profiles in response to therapy. Human T cells and monocytes were recruited to the tumor area and penetrated the entire tumor mass within hours after injection of C242 Fab-SEA. The prodn. of cytokines at the single-cell level was found to be dominated by tumor necrosis factor (TNF)-.alpha., interleukin (IL)-2, IL-4, IL-5, IL-10, IL-12, interferon (IFN)-.gamma., granulocyte-macrophage colony-stimulating factor, and transforming growth factor-.beta., whereas IL-1-.alpha., IL-1ra, IL-1.beta., TNF-.beta., IL-3, IL-6, and IL-8 were undetectable. Most of the TNF-.alpha., IL-2, IL-12, and IFN-.gamma. were made by the infiltrating human leukocytes, while the colon carcinoma cells were induced to produce IL-4, IL-10, and TNF-.alpha.. Up-regulation of IFN-.gamma. receptors and TNF R p60 receptors was found, while the TNF R p80 receptor was absent. The cytokine prodn., T cell infiltration, and CD95 Fas receptor expression concomitantly occurred to induce programmed cell death in the tumor cells. This was followed by a strong redn. of the tumor mass that was seen within 24 h after C242 Fab-SEA infusion. These findings demonstrate that antibody-superantigen proteins efficiently recruit tumor-infiltrating lymphocytes actively producing a variety of cytokines likely to be essential for the therapeutic effects obsd. in the model. Although the humanized SCID model has obvious limitations in its predictive value for treatment of human cancer, we believe that these results encourage clin. evaluation of antibody-targeted superantigens.
IT Toxins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(entero-, A, **conjugate** with antitumor **monoclonal antibody** Fab fragment; **antibody**-targeted superantigen therapy induces tumor-infiltrating lymphocytes, excessive cytokine prodn., and **apoptosis** in human colon carcinoma)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal**, **conjugate** with staphylococcal enterotoxin A; **antibody**-targeted superantigen therapy induces tumor-infiltrating lymphocytes, excessive cytokine prodn., and **apoptosis** in human colon carcinoma)

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 1999 ACS
AN 1996:15530 CAPLUS
DN 124:66620
TI Combination of tumor necrosis-inducing substances with substances activated by necrosis for selective tumor therapy
IN Bosslet, Klaus; Czech, Joerg; Hoffmann, Dieter

PA Behringwerke AG, G[redacted]any
SO Ger. Offen., 4 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4417865	A1	19951123	DE 1994-4417865	19940520
EP 696456	A2	19960214	EP 1995-107299	19950513
EP 696456	A3	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AU 9520151	A1	19951130	AU 1995-20151	19950518
CA 2149818	AA	19951121	CA 1995-2149818	19950519
ZA 9504099	A	19960119	ZA 1995-4099	19950519
US 5710134	A	19980120	US 1995-446211	19950519
JP 07316074	A2	19951205	JP 1995-122483	19950522
PRAI DE 1994-4417865	19940520			

AB The title components may be administered simultaneously, sep., or sequentially for cytostatic therapy of tumors. The tumor necrosis-inducing substance may be (a) a cytotoxic monoclonal antibody specific for tumor endothelium, directed e.g. to the 30.5 kDa antigen or to **apoptosis**-mediating antigen fas of proliferating endothelial cells; (b) a cytotoxic immunoconjugate contg. such an **antibody**; (c) a receptor ligand-toxin **conjugate**; or (d) a tumor metab.-inhibiting substance such as Zilascorb. Enzymes (esp. lysosomal glycosidases) released in response to the necrosis-inducing substance act on the 2nd component, a nontoxic prodrug (e.g. F 826), to produce a toxic drug at high concn. in tumor tissue, resulting in massive tumor cell death.

AB . . . may be (a) a cytotoxic monoclonal antibody specific for tumor endothelium, directed e.g. to the 30.5 kDa antigen or to **apoptosis**-mediating antigen fas of proliferating endothelial cells; (b) a cytotoxic immunoconjugate contg. such an **antibody**; (c) a receptor ligand-toxin **conjugate**; or (d) a tumor metab.-inhibiting substance such as Zilascorb. Enzymes (esp. lysosomal glycosidases) released in response to the necrosis-inducing substance. . .

L4 ANSWER 18 OF 21 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 4
AN 95316066 EMBASE
DN 1995316066
TI The CD4 receptor plays essential but distinct roles in HIV-1 infection and induction of apoptosis in primary bone marrow GPIIb/IIIa+ megakaryocytes and the HEL cell line.
AU Zauli G.; Catani L.; Gibellini D.; Re M.C.; Milani D.; Borgatti P.; Bassini A.; La Placa M.; Capitani S.
CS Institute of Human Anatomy, University of Ferrara,44100 Ferrara, Italy
SO British Journal of Haematology, (1995) 91/2 (290-298).
ISSN: 0007-1048 CODEN: BJHEAL
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
025 Hematology
LA English
SL English
AB We investigated whether cells belonging to the megakaryocytic lineage could be infected in vitro with human immunodeficiency virus type-1 (HIV-1). Primary GPOIIb/IIIa+ bone marrow (BM) cells and HEL continuous cell line were first phenotypically characterized for the presence of megakaryocytic markers and CD4 antigen, then challenged in vitro with the laboratory strain IIIB of HIV-1. Both GPIIb/IIIa+ BM and HEL cells expressed significant levels of CD4 receptor (>50%) and were efficiently infected with HIV-1, as judged by the presence of proviral DNA after polymerase chain reaction analysis and by quantitative evaluation of gag

p24 antigen in the culture supernatants. Of note, infection with HIV-1 in both primary BM megakaryocytes and HEL cells was specifically blocked by soluble recombinant CD4. To ascertain whether the CD4 receptor was essential for infection of megakaryocytic cells, HEL were subcloned into CD4+ and CD4- cells. Although unfractionated and CD4+ HEL cells were productively infected with HIV-1, CD4- HEL cells could not be infected. Infection of HEL cells did not induce gross cytotoxic effects or a significant increase of **apoptosis**. On the other hand, treatment of unfractionated or CD4+ HEL cells with **crosslinked** recombinant env gp120 or Leu3a anti-CD4 **monoclonal antibody** markedly ($P < 0.01$) increased the degree of **apoptosis** with respect to HEL cells infected with HIV-1 or treated with cross-linked gag p24 or anti-GPIIb/IIIa antibody. Taken together, these data indicate that the CD4 receptor represents the main route of infection in cells belonging to the megakaryocytic lineage. Moreover, an inappropriate engagement of CD4 by either free env gp120 or anti-CD4 monoclonal antibody could be more relevant than a direct infection with HIV-1 in the induction of the frequent BM megakaryocyte abnormalities found in HIV-1 seropositive thrombocytopenic patients.

AB . . . cells could not be infected. Infection of HEL cells did not induce gross cytotoxic effects or a significant increase of **apoptosis**. On the other hand, treatment of unfractionated or CD4+ HEL cells with **crosslinked** recombinant env gp120 or Leu3a anti-CD4 **monoclonal antibody** markedly ($P < 0.01$) increased the degree of **apoptosis** with respect to HEL cells infected with HIV-1 or treated with cross-linked gag p24 or anti-GPIIb/IIIa antibody. Taken together, these. . .

L4 ANSWER 19 OF 21 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 5
AN 1995:316994 BIOSIS
DN PREV199598331294
TI Internalization of antigastric cancer **antibody**-trichosanthin **conjugate** and impact of ras oncogene expression on the **conjugate**-induced **apoptosis** in the target cells.
AU Wang, Fuan; Zhang, Xueyong; Li, Song
CS Lab. Gastroenterol., Xijing Hosp., Xi'an 710032 China
SO Zhonghua Weishengquxue He Mianyixue Zazhi, (1995) Vol. 15, No. 2, pp. 131-134.
ISSN: 0254-5101.
DT Article
LA Chinese
SL Chinese; English
AB Trichosanthin (TCS), a naturally occurring single chain plant toxin, was chemically introduced to an antigastric cancer monoclonal antibody MGb-2 so as to generate an antigastric cancer conjugate MGb-2-TCS. The internalization of MGb-2-TCS and the conjugate-mediated cell death mode were then investigated with gold tracing technique combined with electron microscopy using human gastric cancer cells isolated from surgically resected gastric cancer tissue as the target model. In the meantime, the relationship between the ras oncogene expression and the MGb-2-TCS killing efficiency was also explored. It was found that MGb-2-TCS entered the cell via membrane invaginations, and was transported intracellularly from tubulovesicular structures to multivesicular bodies and finally to lysosomes where it was degraded. Only a small amount of the internalized MGb-2-TCS was seen to be translocated to the cytosol at the tubulovesicle and multivesicular body stages. Ultrastructurally, the MGb-2-TCS-damaged cells showed morphological alterations characteristic of apoptosis, Furthermore, it was identified that MGb-2-TCS-damaged cells exhibited little or no expression of P-21ras while the cells with a moderate to high level of P-21ras remained unaffected. The above findings indicate on one hand that the killing of gastric cancer cells by MGb-2TCS was effected

through activation of apoptosis mechanism, and on the other that the process per se seemed to correlate with the expression status of the ras oncogene.

TI Internalization of antigastric cancer **antibody**-trichosanthin **conjugate** and impact of ras oncogene expression on the **conjugate**-induced **apoptosis** in the target cells.

L4 ANSWER 20 OF 21 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 6
AN 94024032 EMBASE
DN 1994024032
TI Antibody-induced apoptosis in a human leukemia cell line is energy dependent: Thermochemical analysis of cellular metabolism.
AU Wallen-Ohman M.; Lonnbro P.; Schon A.; Borrebaeck C.A.K.
CS Department of Immunotechnology, Lund University, PO Box 7031,Lund S-22007,
Sweden
SO Cancer Letters, (1993) 75/2 (103-109).
ISSN: 0304-3835 CODEN: CALEDQ
CY Ireland
DT Journal; Article
FS 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB The mouse monoclonal anti-BAL antibody induced **apoptosis** in a pre-B acute lymphocytic leukemia cell line within 2 days of incubation, after being **crosslinked** by a secondary **antibody**. The **antibody** specifically recognized a 37 kDa membrane protein that was expressed on a wide spectrum of normal and malignant cells, but induced programmed cell death in only very few of these cells. In this study, we have followed the initial kinetics of the antibody-induced cell death in the human acute lymphocytic leukemia cell line KM-3, by microcalorimetric measurements in conjunction with determination of the cellular proliferation rate and DNA fragmentation. An increase in metabolic activity was observed already after incubating the cells for 20 min with **crosslinked** anti-BAL **antibody**, which was several hours before significant growth inhibition and DNA fragmentation were detected. These data show for the first time that the initiation phase of antibody-induced **apoptosis** is an active, energy-dependent process and not merely an effect of receptor blocking.
AB The mouse monoclonal anti-BAL antibody induced **apoptosis** in a pre-B acute lymphocytic leukemia cell line within 2 days of incubation, after being **crosslinked** by a secondary **antibody**. The **antibody** specifically recognized a 37 kDa membrane protein that was expressed on a wide spectrum of normal and malignant cells, but. . .
rate and DNA fragmentation. An increase in metabolic activity was observed
already after incubating the cells for 20 min with **crosslinked** anti-BAL **antibody**, which was several hours before significant growth inhibition and DNA fragmentation were detected. These data show for
the first time that the initiation phase of antibody-induced **apoptosis** is an active, energy-dependent process and not merely an effect of receptor blocking.

L4 ANSWER 21 OF 21 DPCI COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1996-151333 [15] DPCI
CR 1997-424764 [39]
DNC C1996-047540
TI Immuno-**conjugate** comprising tyrosine kinase inhibitor linked to **antibody** - binds to cell surface receptor of cell with tyrosine kinase activity, used to induce **apoptosis** in target cells, and to treat, e.g. cancers and auto-immune diseases.
DC B04 D16

IN UCKUN, F M
PA (MINU) UNIV MINNESOTA
CYC 65
PI WO 9606116 A1 19960229 (199615)* EN 59p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN
AU 9532168 A 19960314 (199625)
US 5587459 A 19961224 (199706) 34p
EP 776338 A1 19970604 (199727) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 10505056 W 19980519 (199830) 62p
EP 776338 B1 19981209 (199902) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69506561 E 19990121 (199909)
US 5872223 A 19990216 (199914)
ADT WO 9606116 A1 WO 1995-US10123 19950808; AU 9532168 A AU 1995-32168 19950808; US 5587459 A US 1994-293731 19940819; EP 776338 A1 EP 1995-928368 19950808, WO 1995-US10123 19950808; JP 10505056 W WO 1995-US10123 19950808, JP 1996-508124 19950808; EP 776338 B1 EP 1995-928368 19950808, WO 1995-US10123 19950808; DE 69506561 E DE 1995-606561 19950808, EP 1995-928368 19950808, WO 1995-US10123 19950808; US 5872223 A Cont of US 1994-293731 19940819, US 1996-755462 19961122
FDT AU 9532168 A Based on WO 9606116; EP 776338 A1 Based on WO 9606116; JP 10505056 W Based on WO 9606116; EP 776338 B1 Based on WO 9606116; DE 69506561 E Based on EP 776338, Based on WO 9606116; US 5872223 A Cont of US 5587459
PRAI US 1994-293731 19940819; US 1996-755462 19961122
TI Immuno-**conjugate** comprising tyrosine kinase inhibitor linked to **antibody** - binds to cell surface receptor of cell with tyrosine kinase activity, used to induce **apoptosis** in target cells, and to treat, e.g. cancers and auto-immune diseases.